

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) An *in vitro* method for the production of a homologous heart valve, comprising the steps of:

- a) providing a biodegradable support comprising a broad edge,
- b) colonizing the support with homologous fibroblast or myofibroblast cells or a combination thereof to form a connective tissue matrix,
- c) optionally colonizing the connective tissue matrix with endothelial cells, and
- d) fixing the connective tissue matrix to a ~~non-degradable or poorly slowly~~ degradable frame construction,

wherein, before or after the fixing of the frame construction, the connective tissue matrix optionally colonized with endothelial cells is introduced into a pulsatile flow chamber in which it can be exposed to increasing flow rates, wherein the flow rate is increased continuously or discontinuously, wherein the broad edge is a suture ring, wherein the biodegradable support begins degrading at least 8 days post colonization and is completely degraded no later than 3 months after colonization, and wherein the ~~poorly slowly~~ degradable frame does not degrade prior to a year after colonization.

2. (currently amended) An *in vitro* method for the production of a homologous heart valve, comprising the following steps:

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/523,618 (Q117058)

- a) providing a biodegradable support which is firmly connected to a ~~non-degradable or poorly~~slowly degradable frame construction, wherein the biodegradable support comprises a broad edge, and wherein the broad edge is a suture ring,
- b) colonizing the support with homologous fibroblast or myofibroblast cells or a combination thereof to form a connective tissue matrix,
- c) optionally colonizing the connective tissue matrix with endothelial cells,
- d) introducing the frame construction with the connective tissue matrix connected thereto into a pulsatile flow chamber in which it can be exposed to increasing flow rates, and
- e) continuously or discontinuously increasing of the flow rate,

wherein the biodegradable support begins degrading at least 8 days post colonization and is completely degraded no later than 3 months after colonization and wherein the ~~poorly~~slowly degradable frame does not degrade prior to a year after colonization.

3. (previously presented) The method according to claims 1 or 2, wherein the biodegradable support comprises a biodegradable polymer matrix or an acellular biological matrix.

4. (previously presented) The method of claim 3, wherein the support comprises a polyglycolic acid (PGA), polylactic acid (PLA), polyhydroxyalkanoate (PHA), poly-4-hydroxybutyrate (P4HB) or a mixture of two or more of these polymers.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/523,618 (Q117058)

5. (previously presented) The method according to claims 1 or 2, wherein the support has a polymer density of 40 to 120 mg/cm³.

6. (previously presented) The method according to claims 1 or 2, wherein the support comprises a porous polymer having a pore size of 80 to 240 μm.

7. (previously presented) The method according to claims 1 or 2, wherein the fibers of the support have a diameter of 6 to 20 μm.

8. (previously presented) The method of claim 3, wherein the support comprises an acellular connective tissue framework of an animal or human heart valve.

9. (previously presented) The method according to claims 1 or 2, wherein the step of colonization with fibroblast or myofibroblasts cells or a combination thereof repeated 3 to 14 times.

10. (previously presented) The method according to claims 1 or 2, wherein approximately 10⁵ to 6 × 10⁸ fibroblast or myofibroblast cells or a combination thereof are employed per square centimeter of support.

11. (previously presented) The method according to claims 1 or 2, wherein the step of colonization with endothelial cells is repeated 3 to 14 times.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/523,618 (Q117058)

12. (previously presented) The method according to claims 1 or 2, wherein approximately 10^5 to 5×10^8 endothelial cells are employed per square centimeter of support.
13. (previously presented) The method according to claims 1 or 2, wherein the cells are human cells.
14. (previously presented) The method according to claims 1 or 2, wherein the cells are autologous cells.
15. (previously presented) The method according to claims 1 or 2, wherein the frame construction comprises a biocompatible material.
16. (cancelled).
17. (previously presented) The method according to claims 1 or 2, wherein the support is fixed to the frame construction by means of conventional suturing, fibrin adhesive, or a combination thereof.
18. (previously presented) The method according to claims 1 or 2, wherein flow rates of 5 ml/min to 8,000 ml/min are established in the pulsatile flow chamber.
19. (previously presented) The method according to claims 1 or 2, wherein the flow rate is increased over a period of 1 week to 12 weeks.

AMENDMENT UNDER 37 C.F.R. § 1.111
U.S. Application No. 10/523,618 (Q117058)

20. (previously presented) The method according to claims 1 or 2, wherein the initial flow rate is 50 to 100 ml/min.

21. (previously presented) The method according to claims 1 or 2, wherein the initial pulse frequency is 5 to 10 pulses/min.

22. (previously presented) The method according to claims 1 or 2, wherein the flow rate is increased to 5,000 ml/min.

23. (previously presented) The method according to claims 1 or 2, wherein the pulse frequency is increased to 180 pulses/min.

24. (previously presented) The method according to claims 1 or 2, wherein systemic pressures of 10 to 240 mm Hg are established in the pulsatile flow chamber.

25. (previously presented) An autologous heart valve that has been produced by the method according to claims 1 or 2.

26. (currently amended) An autologous heart valve having a connective tissue inner structure surrounded by an endothelial cell layer, wherein the connective tissue inner structure is fixed to a ~~non-degradable or~~ slowly degradable frame construction, wherein the frame construction comprises a broad edge wherein the broad edge is a suture ring, wherein the biodegradable support begins degrading at least 8 days post colonization with the endothelial cell

layer and is completely degraded no later than 3 months after colonization with the endothelial cell layer and wherein the ~~poorly~~slowly degradable frame does not degrade prior to a year after colonization with the endothelial cell layer.

27. (previously presented) The autologous heart valve according to claim 26, wherein a collagen density of 20 to 60 % exists in the connective tissue inner structure.

28. (previously presented) The autologous heart valve according to claim 27, wherein the heart valve withstands the flow conditions in the human heart.